Quinoline is a nitrogen-containing heterocyclic compound with molecular formula C₉H₇N and molecular weight 129.16. Quinoline is used as a lead compound in which the benzene ring is fused with the pyridine ring on the 2-3 position. The heterocyclic ring is a pharmacophore of significant importance. Replacement of this ring results in the loss of pharmacological activity. The quinoline nucleus is a ubiquitous structural motif found in many naturally occurring quinoline alkaloids.

Tyrosine kinase (PDGF-RTK) inhibitor, DNA-intercalating carrier, analgesic, anti-HIV, anti-tumor, DNA binding capability, and many other functional materials.

Quinoline has been found to possess anti-malarial, anti-bacterial, anti-fungal, anti-helmintic, cardiotonic, anti-convulsant, anti-inflammatory & analgesic activity. A wide variety of substituted quinoline derivatives posses a broad range of bio-activities like anti cancer, antibiotic, anti-hypertensive, platelet-derived growth factor receptors, tyrosine kinase (PDGF-RTK) inhibitor, DNA-intercalating carrier, analgesic, anti-HIV, anti tumor, DNA binding capability, and many other functional materials.

COUMARIN: Coumarin (benzopyrones) is a compound containing two rings of six members heterocycle rings with two oxygen atoms. Classification of Coumarins includes simple coumarin, furanocoumarins, pyranocoumarins and coumarins substituted in the pyrone ring. Simple coumarins are compounds that undergo hydroxylation, alkoxylation, and alkylation to form its derivatives. For furanocoumarins, these compounds consist of five members furan ring attached to the coumarin core. Pyranocoumarins are a compound that contained a linear or angular type with substituents on benzene and pyrone rings.

CHALCONE: Chalcone is a generic term for the compounds bearing the 1,3-diphenyl-1-prop-2-ene-1-one framework. Under homogeneous conditions, these compounds are usually prepared by base or acid catalyzed aldol condensation between aromatic aldehydes and ketones.
represent an important compounds due to their chemical flexibility, as synthons for the production of five and six-members ring systems for example Pyrazoles Pyrazolines, isooxazolines, aurones, Pyrimidine, falvanones and di-aryl cyclohexenones. The biological activities of chalcones are equally wide ranging. In fact, not many structural templates can claim association with such a diverse range of pharmacological activities, among which among antimicrobial, antileishmanial, anti-malarial, antifungal, anti-oxidant, chemo preventive activity, anti-proliferative activity and anti-HIV activity, antitumour, anti-inflammatory, analgesic and antipyretic, bactericidal, antifungal and insecticidal activity, antimutagenic, antileishmanial, are widely cited.

**MATERIALS AND METHOD**

**MATERIALS**

All chemicals used were of analytical grade from, SD Fine. Melting points of all the synthesized compounds were determined by open capillary tube method. These are uncorrected. The purity of all compounds was checked by TLC was run on Silica Gel G plates using Chloroform and Ethanol (9:1). Spots were visualized using iodine vapour chamber. IR spectra were recorded on Shimadzu IR spectrophotometer by using KBr pellets technique. 1H- NMR was recorded on Bruker AMX 60 MHz spectrophotometer by using DMSO as solvent.

**METHODOLOGY:**

**Step-1: Preparation of 2-chloroquinoline-3-carbaldehyde derivatives:**

DMF (9.13gm, 0.125M) was cooled to 0°C in a flask equipped with drying tube and phosphorous oxychloride (53.7gm, 32.2 mL) was added drop wise with stirring to this solution various substituted acetanilide (0.05 mole) was added and after 5 min the solution was heat under reflux for 16 hrs. The reaction mixture was poured into ice water (300ml) and stirred for 30 min at 0-10°C when 2-chloro-3-formyl quinoline separated as yellow precipitate. It was filtered washed with water and recrystalized from ethyl acetate into yellow needles M.P-145°C yield 66.94%.

**Step-2: Preparation of 3-Acetyl Coumarin:**

Equimolar mixture of Salicylaldehyde (0.01 mole) and ethyl aceto acetate (0.01 mole) stir at room temperature and add few drops of piperidine. A pale yellow viscous precipitate is formed neutralize it with 1N Hcl. The obtained product is separated by filtration, dried and recrystallized by ethanol.

**Step-3: Formation of Coumarin containing Quinoline derivatives (chalcones):**

Take equimolar mixture (0.005mole) of 2-chloro-3-formyl quinoline derivatives and (0.005mole) of 3-acetyl coumarin. Dissolve the mixture in 15ml ethanol to this add 15ml of 40% KOH. Irradiation in microwave for 50-70 sec, product was filtered and dried. Completion of reaction was monitored by using TLC.

Purification of derivatives was done by recrystallization using ethanol.

**Synthetic scheme:**

![Synthetic scheme](image-url)
SPECTRAL ANALYSIS:

3-(3-(2-chloroquinolin-3-yl) acryloyl)-2H-chromen-2-one (5a) IR (KBr)cm⁻¹: Aromatic C-H Str 3066.82, Aliphatic C-H Str 2978.09, Ketone C=O Str 1620.21, 1610 C=N Str 1489.05, C-O-C Str 1138, C-Cl Str 597.93; 1H NMR dppm 6.0 CH=CH (s, 2H), 7.1-8.7 Ar-H (m, 9H); Mass spectra: [M+H⁺] = 362

3-(3-(2-chloro-6-carboxy quinolin-3-yl) acryloyl)-2H-chromen-2-one (5b) IR (KBr)cm⁻¹: Aromatic C-H Str 3021.33, Aliphatic C-H Str 2978.09, Carboxylic OH Str 2920.23Ketone C=O Str 1620.21, COOH 1635.64Ketone C=O 1620 C=N Str 1458.11, C-O-C Str 1103.28, C-Cl Str 597.93; 1H NMR dppm 6.2 CH=CH (s, 2H), 7.1-8.3 Ar-H (m, 9H), 12.6 COOH; Mass spectra: [M+H⁺] = 406

3-(3-(2-chloro-6-methyl quinolin-3-yl) acryloyl)-2H-chromen-2-one (5c) IR (KBr)cm⁻¹: Aromatic C-H Str 3032.99, Aliphatic C-H Str 2920.23, Ketone C=O 1635.64, 1610 C=N Str 1458.18, C-O-C Str 1107.14, -CH₃ Str 1384.89; 1H NMR dppm 6.1 CH=CH (s, 2H), 7.1-8.3 Ar-H (m, 9H), 2.5 CH₃ (s, 1H); Mass spectra: [M+H⁺] = 376

3-(3-(2-chloro-6-nitro quinolin-3-yl) acryloyl)-2H-chromen-2-one (5d) IR (KBr)cm⁻¹: Aromatic C-H Str 3056.70, Aliphatic C-H Str 2919.87, Ketone C=O Str 1638.59, 1610 C=N Str 1444.40, Amide (N-H) Str 3251.46; 1H NMR dppm 4.6 CH=CH (s, 2H), 7.0-8.3 Ar-H (m, 9H); Mass spectra: [M+H⁺] = 406

3-(3-(2-chloro-8-hydroxy quinolin-3-yl) acryloyl)-2H-chromen-2-one (5e) IR (KBr)cm⁻¹: Phenolic OH Str 3444.87, Aromatic C-H Str 3066.82, Aliphatic C-H Str 2978.09, Ketone C=O Str 1639.49, 1600 C=N Str 1458.18, C-O-C Str 1103.28, C-Cl Str 570.93; 1H NMR dppm 5.0 CH=CH (s, 2H), 7.1-8.5 Ar-H (m, 9H), OH (s, 1H) 4.5; Mass spectra: [M+H⁺] = 376

BIOLOGICAL SCREENING

In vitro Anti-malarial Activity:

In this research work, firstly, all the derivatives were subjected to the susceptibility assay for *Plasmodium falciparum* to find out whether the synthesized derivatives possess anti-malarial activity or not. In this point of view, schizonticidal testing method was selected based on the ease of the test, less time consumption, robust, and economical. Further to support the selection of schizonticidal as the test assay for the synthesized derivatives, schizonticidal possess the anti-malarial susceptibility of the derivatives.

**Figure 1:** Pie diagram representation

**Schizonticidal testing of synthetic compound**

- The sample is dissolved in dimethylsulphoxide (DMSO) at 100mg/ml concentration. The repetitive dilutions were prepared in incomplete RPMI-1640 media (pH 7.2) up to 2mg/ml concentration.
- Add initial 100µl incomplete media in all eight wells of the vertical line of 96-tissue culture well plate.
- From 2mg/ml concentration 100 µl was loaded in the third well of 96-tissue culture well plate. The first well was of control containing only infected blood with medium.
- Second well was of experimental control having DMSO dilution without drug to know the level of inhibition through DMSO.
- Second well was of experimental control having DMSO dilution without drug to know the level of inhibition through DMSO.
- From third to eight well proceed with double dilution method. The range of samples concentration after double dilution from 3rd to 8th well was 0.1 to 0.003 mg/well (i.e. 1 to 0.03mg/ml).
- Finally add 10(0.1 synchronized culture in each well.
- Close the plate and put in incubation for 36 hrs for the development of schizonts from rings.
- In between 36 to 40 hrs opened the plate and removed the media and prepared slides from all wells.
Table 2: Inhibitory Concentration IC(mg/ml)

<table>
<thead>
<tr>
<th>Compounds</th>
<th>Inhibition of Schizont maturation at various con. In (%) mg/ml</th>
<th>Inhibitory con. (mg/ml) –IC-50</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.5 0.25 0.125 0.063 0.03125</td>
<td>log 2x= logex/0.69</td>
</tr>
<tr>
<td>5a</td>
<td>52 46 29 16 9 2</td>
<td>0.9</td>
</tr>
<tr>
<td>5c</td>
<td>51 40 19 12 11 5</td>
<td>0.9</td>
</tr>
<tr>
<td>5d</td>
<td>58 49 32 20 13 8</td>
<td>1.2</td>
</tr>
<tr>
<td>Chloroquine Phosphate</td>
<td>71 24 21 19 12 8</td>
<td>0.5</td>
</tr>
</tbody>
</table>

RESULTS AND DISCUSSION
In the present research work, based on the wide literature survey, novel derivatives of coumarin containing quinoline derivatives were synthesized in three-step facile procedure and five in number. All the reactions were monitored by TLC and purification was done by recrystallization process. All the derivatives were characterized using spectral studies like FT-IR spectroscopy, ¹H-NMR spectroscopy and Mass spectrometry.

From all the five derivatives three were screened for their in-vitro anti-malarial activity using schizonticidal testing method by using...
chloroquine phosphate as standard. The anti-malarial activity of the synthesized derivatives, 5a, 5c & 5d was carried out using schizonticidal testing method against *plasmodium falciparum* (RPMI-1640 strain (10.4 g/1) at various concentrations from 1 to 0.03125 mg/ml (1, 0.5, 0.25, 0.125, 0.063 and 0.03125 mg/ml). Out of all the three synthesized compounds, except 5a, remaining two derivatives showed good to excellent activities with similar minimum inhibitory concentrations compared to that of the standard drug chloroquine phosphate. The order of anti-malarial activity of the synthesized compounds is as follows:

5a > 5c > 5d

**CONCLUSION**

Five Novel coumarin containing quinoline derivatives were synthesized by both conventional method and microwave techniques. All the synthesized compounds were characterized by physical (TLC and M.P) and spectral data (IR, NMR, and MASS). The most effective anti-malarial activity was shown by 5d due to the presence of nitro group at para position, but significant activity when compared to the standard, chloroquine phosphate. This promising antimalarial *in vitro* results also gives scope for further comparing the selected derivatives’ *in vitro* results with *in vivo* and if possible with *in vivo* results also for confirming the potency of the derivatives against malaria.

**ACKNOWLEDGEMENT**

The authors are thankful to the secretary Sri. C. Gangi Reddy Garu through the principal, Annamacharya college of pharmacy, Rajampet for providing necessary facilities to carry out the research work.

**REFERENCES**


Source of support: Nil, Conflict of interest: None Declared